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10/505,393	08/20/2004	Mitsuaki Kuwano	04561/HG	7247

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FRISHAUF, HOLTZ, GOODMAN & CHICK, PC
220 Fifth Avenue
16TH Floor
NEW YORK, NY 10001-7708

EXAMINER	
ELLIS, SUEZU Y	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,393	KUWANO ET AL.	
	Examiner	Art Unit	
	Suezu Ellis	2876	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-10,12-14,16 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-10,12-14,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/08, 7/11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL REJECTION

Response to Arguments

Applicant's arguments with respect to claims 1-4, 6-10, 12-14, 16 and 17 have been considered but are moot in view of the new ground(s) of rejection.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on April 14, 2008 and July 11, 2008 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

The disclosure is objected to because of the following informalities:

On pg. 6, 4th line from the bottom, the term "antimicrovial" is used. The spelling appears to be incorrect – the proper spelling should be "antimicrobial"

Appropriate correction is required.

Claim Objections

Claims 1, 2, 7, 12 and 17 are objected to because of the following informalities:

Claims 1 and 2 recite the terms "subjuntival" and "subjunctivally", respectively. The spelling appears to be incorrect – the proper spelling should be "subconjunctival" and "subconjunctivally", respectively.

Claims 7, 12 and 17 recite the word "antimicrovial". The spelling appears to be incorrect – the proper spelling should be "antimicrobial"

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 8-10, 12 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating uveitis, cytomegalovirus retinitis, diabetic retinopathy, proliferative vitreretinopathy, and retinal detachment but does not reasonably provide enablement for the treatment of age-related macular degeneration, retinitis pigmentosa, central retinal vein occlusion, or central retinal artery occlusion. Further, the specification does not reasonably provide enablement for the prevention of uveitis, cytomegalovirus retinitis, age-related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinal detachment, retinitis pigmentosa, central retinal vein occlusion, and central retinal artery occlusion. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The art has reasonably demonstrated/disclosed that fine particle injection of drugs including betamethasone, dexamethasone, triamcinolone, and prednisolone may

be useful for treating uveitis, diabetic retinopathy, proliferative vitreretinopathy, and retinal detachment. However, the claims also encompass using fine particle injection of drugs including betamethasone, dexamethasone, triamcinolonne, and prednisolone for the treatment of age- related macular degeneration, retinitis pigmentosa, central retinal vein occlusion, or central retinal artery occlusion and the prevention of uveitis, cytomegalovirus retinitis, age-related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinal detachment, retinitis pigmentosa, central retinal vein occlusion, and central retinal artery occlusion which is clearly beyond the scope of the instantly disclosed/claimed invention.

Please note that the term "prevent" is an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does "therapeutic" or "treat", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination regimes) - including preventing such disorders as Age-related Macular Degeneration, which is clearly not recognized in the medical art as being a totally preventable condition.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (Wands, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the

art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7)the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to the prevention of uveitis, cytomegalovirus retinitis, age-related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinal detachment, retinitis pigmentosa, central retinal vein occlusion, and central retinal artery occlusion by subconjunctivally administering a fine particle injection of drugs such as betamethasone, dexamethasone, triamcinolonne, and prednisolone. Thus, the claims taken together with the specification imply that the listed ocular conditions are preventable with a fine particle injection of drugs such as betamethasone, dexamethasone, triamcinolonne, and prednisolone administered subconjunctivally.

The claims are drawn to the treatment of age-related macular degeneration, retinitis pigmentosa, central retinal vein occlusion, or central retinal artery occlusion by subconjunctivally administering a fine particle injection of drugs such as betamethasone, dexamethasone, triamcinolonne, and prednisolone. Thus, the claims taken together with the specification imply that all the listed ocular conditions are treatable with the subconjunctival administration of a fine particle injection of drugs such as betamethasone, dexamethasone, triamcinolonne, and prednisolone.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The Merck Manual addresses CMV retinitis typically affects HIV-infected patients and rarely organ transplant recipients and other immunocompromised patients. The infection is treated with anti-viral, typically ganciclovir, valacyclovir, or valganciclovir. Corticosteroids are not given and would be contraindicated as they are immunosuppressant which would advance the CMV virus further.

The Merck Manual also teaches that retinitis pigmentosa is progressive and bilateral degeneration of the retina and pigmented epithelium of the choroid. The condition has an incomplete understanding of the etiology which does not allow for prevention. There is also no treatment.

The Merck Manual teaches that uveitis is typically idiopathic and which cannot be prevented and there is no consistent cause. Some identifiable causes are infections and trauma which are not preventable. The condition can be treated with drugs including corticosteroids.

The Merck Manual teaches that central retinal artery occlusion is usually by embolisms which are not known in the art to be preventable and the treatment does not include ocular injection. Additionally teaches that central retinal vein occlusion is by a thrombus or idiopathic which are not known in the art to be preventable and most treatments are ineffective or unproven. There is no generally accepted medical therapy.

Schmidt-Erfurth (Management of neovascular age-related macular degeneration) addresses Age-related Macular Degeneration and how only recently gaining new insights in the pathogenesis of the disease are allowing for improved treatment for the

management of the disease, not prevention as the etiology is still not clear for those skilled in the art.

(5) The relative skill of those in the art:

The relative skill is high.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for formulating the drug particles, injecting the particles to the eye of rabbits, and the presence of the drug in the eye upon evaluation.

However, the specification does not provide for any method of treatment nor of prevention for any condition.

There are no working examples for treatment for any of the claimed conditions. As several of the claimed conditions do not share a common etiology, and there is no guidance or working examples to show how to use the invention with a reasonable expectation of success to treat these conditions. The art provides for the use of a fine particle injection of drugs including betamethasone, dexamethasone, triamcinolonne, and prednisolone for treating uveitis, diabetic retinopathy, proliferative vitreretinopathy, and retinal detachment only. Additionally, the specification does not provide for prevention of any conditions listed.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to prevention of the ocular conditions, treatment of the

conditions listed, and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Gwon et al. (US 5,300,114)

With respect to claim 1, Gwon et al. discloses a drug delivery system (subconjunctival implant) to a posterior segment of an eye comprising fine particles containing a drug which are subconjunctivally administered, wherein the posterior segment of the eye is a retina, choroid, vitreous body or a crystalline lens (col. 4, lines 58-60; col. 5, lines 3-10).

With respect to claims 6 and 7, Gwon et al. discloses the drug is an antiviral (gangcyclovir) for treating cytomegalovirus retinitis (col. 5, lines 18-20).

Claims 1, 2, 4, 6-8, 10, 12, 14, 16 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Peyman (US 6,395,294).

With respect to claims 1 and 2, Peyman discloses a drug delivery system (subconjunctival injection) to a posterior segment of an eye comprising fine particles containing a drug which are subconjunctivally administered, wherein the posterior segment of the eye is a vitreous body (col. 3, lines 12-27, 36-43; col. 4, lines 23-24, 33-46).

With respect to claim 8, Peyman discloses a method of treating a disease of a posterior segment of an eye (a surgical method to alleviate a structural disorder of the eye caused by the vitreous) comprising subconjunctivally administering to a patient an effective amount of an injection comprising fine particles containing a drug. Peyman discloses the structural disorder of the eye caused by the vitreous is uvetis, cytomegalovirus retinitis, age-related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinal detachment, pigmentary retinal degeneration, central retinal vein occlusion or central retinal artery occlusion (col. 1, lines 14 - col. 2, line 25; col. 3, lines 12-27, 36-43; col. 4, lines 23-24, 33-46, 58-62).

With respect to claims 4, 10 and 14, Peyman discloses the therapeutic agent may be incorporated into a vesicle such as a microsphere made of polyglycolic or

polylactic acid (biodegradable polymer) (col. 2, lines 52-54; col. 3, lines 36-42; col. 5, lines 38-44).

With respect to claims 6, 7, 12, 16 and 17, Peyman discloses the drug can be dexamethasone (anti-inflammatory/immunosuppressor), or triamcinolone, or betamethasone (anti-inflammatory/immunosuppressor) (claim 1; col, 4, lines 45-46, 58-61; col. 5, lines 4-19), which are the same drugs disclosed in the instant application. Therefore the drug is considered to be a drug for treatment/prevention of uvetis, cytomegalovirus retinitis, age-related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinal detachment, pigmentary retinal degeneration, central retinal vein occlusion or central retinal artery occlusion.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peyman in view of Ogura et al. (JP 2000-247871).

With respect to claims 3, 9 and 13, Peyman addresses all the limitations of claims 1, 2 and 8, and further discloses the particle size being less than 50 μm, therefore can overlap with the claimed range of 50 nm to 150 μm. (col. 4, lines 23-24). Ogura et al. teaches a drug release control system for treating various diseases of a

retina or vitreous body wherein the drug has a particle diameter in the range of 50-200 nm [0009], [0021], [0022]. It would have been obvious to one of ordinary skill in the art to modify the particle size of the drug, as desired, in order to provide a controlled release of the drug in the retina (drug emission control over a long period of time) [0016]. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or working ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Telephone/Fax Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suezu Ellis whose telephone number is (571) 272-2868. The examiner can normally be reached on 8:30am-5pm (Monday-Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SE

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615